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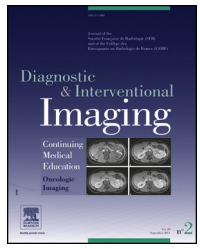

CONTINUING EDUCATION PROGRAM: FOCUS...

Correlation between MRI and biopsies under second look ultrasound

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KEYWORDS
Breast;
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Second look ultrasound

Abstract The term ''second look'' lesions in MRI refers to lesions detected by MRI that were not initially seen on mammography or ultrasound. The objectives of our study were to analyse the displacement of targets between MRI and ultrasound; to define discriminating BIRADS morphological criteria to predict benign or malignant character and better establish the indications of second look ultrasound and biopsy; and to analyse the agreement between ultrasound and MRI in terms of morphological criteria. A retrospective and monocentric review was performed of the records of consecutive patients with breast abnormalities (mass or non-mass) initially detected by MRI that were not initially seen on mammography or ultrasound. All patients with abnormalities found during the performance of second look ultrasound and biopsied were included in the study. All lesions were documented using the BIRADS lexicon for MRI and ultrasound. Of 100 included patients, 108 lesions were detected by MRI, found *via* second look ultrasound and biopsied between January 2008 and 2010. All of the included patients were followed-up for a variable period, from 2 to 5 years. Eighty-two upon 108 biopsied lesions (76%) were benign and 26/108 lesions (24%) were malignant. This study confirmed the switch from procubitus to decubitus essentially displaces the tumour in the antero-posterior direction. It showed that the risk factors were not reliable criteria for establishing an indication for second look ultrasound. This study also showed that circumscribed contours and a progressive enhancement curve (type I) for masses on MRI had the strongest negative predictive value of greater than 0.85. In ultrasound,

Abbreviations: IDC, Invasive ductal carcinoma; ILC, Invasive lobular carcinoma; DCIS, Ductal carcinoma *in situ*; MRI, Magnetic resonance imaging; MPR, Multi planar reconstruction; LEQ, Lower external quadrant; LIQ, Lower internal quadrant; UEQ, Upper external quadrant; UIQ, Upper internal quadrant; NME, Non-masslike enhancement; JEQ, Junction of the external quadrants; JLQ, Junction of the lower quadrants; JIQ, Junction of the internal quadrants; UQS, Junction of the upper quadrants.

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the round or oval shape, circumscribed contours and the parallel orientation to the skin favoured benignity with a NPV of greater than 0.85. For masses, the study showed that the agreement in interpretation of the benign versus suspicious morphological criteria between the MRI and the ultrasound was very weak for the shape (Kappa = 0.09) and weak for the contours (Kappa = 0.23). Finally, the MRI overestimated the size of the targets compared to ultrasound (Student *t*-test, $p = 0.0001$). The performance of second look ultrasound has to be performed after the detection of an abdnormality on MRI even for lesion classified BIRADS 3. The biopsy indications must be wide with insertion of a clip and a control MRI. Only this control allows to stop the investigation if the biopsied lesion is benign.

Introduction

The term ''second look'' lesions in MRI refers to lesions detected by MRI that were not initially seen on mammography or ultrasound. In a recent meta-analysis evaluating the role of MRI in the detection of these additional tumours in the homolateral breast, the prevalence of detection was approximately 16% (between 6 and 34%) with a positive predictive value of 66% [1]. A histological control is therefore often useful when faced with the discovery of additional new lesions by MRI before choosing a treatment in order to reduce false positives and to avoid useless mastectomies in case of falsely malignant additional lesions.

Compared to MR-guided biopsies, ultrasound-guided biopsies are easier, faster, less expensive, more accessible (fewer MRI machines), less anatomically limited (deep and axillary internal lesions) and more comfortable for the patients. In addition, biopsies performed under MRI do not allow for real time control during biopsy. The underestimation rate of MR-guided biopsies of risky lesions such as atypical ductal hyperplasia could be 38%, *i.e.* 18% higher than under stereotaxis [2].

We therefore looked at the performance of second look ultrasound based first on the review of the literature and second on the data from a retrospective study concerning:

- the analysis of the displacement of targets between MRI and ultrasound;
- screening for discriminating BIRADS morphological criteria to predict benign or malignant character and better establish the indications of second look ultrasound and biopsy;
- the analysis of the agreement between ultrasound and MRI in terms of morphological criteria.

Patients and methods

Patients

A retrospective study was conducted at the Saint Louis University Hospital Centre. Between January 2008 and 2010, all patients who had a breast MRI detecting an abnormality that was not seen during a prior evaluation including mammography and/or ultrasound found during the performance of second look ultrasound and biopsy were included in the study. No calcification or mass-type abnormalities were found on the mammography in the corresponding region and there was no obvious palpable lesion. Hundred consecutive patients were included according to these inclusion criteria. The indications for breast MRI were as follows: pre-treatment evaluation of breast cancer (invasive lobular carcinoma or locally advanced invasive ductal carcinoma) confirmed by histology ($n = 41/100$), screening of patients with a family history with more than three affected family members ($n = 19/100$, including 5 BRCA1/2 patients), monitoring of patients with a personal history of breast cancer ($n = 15/100$), exploration of an abnormality detected by mammography or ultrasound ($n = 15/100$), exploration of a clinical abnormality such as axillary adenopathy (n = 3/100), nipple retraction (n = 5/100) or breast discharge ($n = 2/100$) without an abnormality found by initial ultrasound or mammography. All of the patients included in the study had a clinical examination, mammography and ultrasound before the MRI. Lesions that were already known before the MRI were excluded from the study. Only the lesions that had not been detected by the clinical examination, mammography and ultrasound were included in the study. The age of the included patients was between 29 and 79 years, with a mean age of 48.9 years.

MRI

All the patients had a bilateral breast MRI on the same MRI machine (MRI 1.5 Tesla, Siemens Symphony TIM, Erlangen, Germany), but the protocol followed was not always exactly the same. However all of the protocols included an axial T2 sequence with or without saturation of the fat signal (TR msec/TE msec, 1300/242; ETL 189, matrix, 384×384; FOV, 320×320 mm; jointed cuts, 1.2 mm), and dynamic axial T1 sequences without and then with injection of contrast material (Dotarem®, Guerbet, France) with MPR and MIP reconstruction and subtraction (TR msec/TE msec, 4.67/1.65; flip angle, 12°; matrix, 320×320; FOV, 380×320 mm; jointed cuts, 1.2 mm).

All of the MRIs were reread by two radiologists (1 and 10 years of experience in breast MRI) for inclusion in the study and based on the BIRADS lexicon. The detected lesions all had enhancement abnormalities: focal lesion, mass and non-mass. For the masses, the size, exact location (quadrants, hour, depth, distance with regard to the nipple), form (round, oval or irregular), contours (circumscribed, irregular and spiculated), the kind of internal enhancement (homogeneous, heterogeneous, existence of non-enhanced septa and annular enhancement, as well as the curve type) and the

BIRADS were described. For non-masses, their distribution (focus, focal area, linear-type non-masslike enhancement, segmentary, regional, diffuse) as well as their internal enhancement (homogeneous, heterogeneous, homogeneous or annular micronodular character) and the BIRADS classification were described.

Of these 100 patients, 108 lesions were detected by MRI and found on the second look ultrasound.

Second look ultrasound

All of the patients had a targeted second look ultrasound (Aixplorer®, Supersonic Imaging, France) within a mean of 4 days. It should be noted that 42 of 100 patients had second look ultrasound immediately after the performance of the MRI. The lesion(s) detected by MRI and found on the ultrasound were described by the operator at the time of the performance of the ultrasound as per the BIRADS terminology. The location of the mass (quadrant, depth, hour), its size, shape (round, oval, irregular), contours (circumscribed, irregular, spiculated), orientation (vertical, horizontal), echogenicity (hypo/iso/hyperechogenic, heterogenic), the existence of acoustic particularities (attenuation, reinforcement) as well as the BIRADS classification were described. Following the second look ultrasound, the detected lesion(s) were all biopsied. The mean time between the performance of the MRI and the biopsy was 10.1 days.

For each biopsied lesion, two to four samples were taken using a 16 to 14 G coaxial system. One in two samples was fixed in alcohol formalin acetic acid (AFA), and the other half of the samples was frozen in liquid hydrogen. The samples were all analysed at the Saint Louis hospital by the same pathologist (20 years of experience in breast pathology). The histological and anatomical pathology information was collected from reports primarily with the malignant or benign nature of the biopsied abnormality. For the benign lesions, we distinguished between the following diagnoses: healthy breast tissue, adenofibroma, fibrocystic dystrophy, fibrous restructuring, papilloma/papillary cystadenoma without atypia, other benign pathologies (adenosis, cylindrical metaplasia, intra-epithelial/intra-ductal/lobular hyperplasia without atypia, desmoid fibroma) and hyperplasia with atypia. For malignant lesions, we distinguished between the type of carcinoma (invasive or *in situ* lobular/ductal), the grade and the existence of hormone receptors (oestrogen and progesterone) as well as the overexpression or non-overexpression of CerB2. For operated lesions, the concordance between the histological examination of the biopsy samples and that of the removed piece was checked.

Follow-up

All of the included patients had biopsies and were then followed-up for a variable period after their biopsy (from 2 to 5 years) with different imaging modalities (mammography, ultrasound or MRI) according to their personal and family medical histories and the nature of the lesions identified on the MRI that were biopsied. In all cases, the follow-up modalities included at least one clinical examination, and most often a control mammography or ultrasound in combination or not in combination with MRI.

Statistics

The statistics were performed using the Analyse-It software programme (United Kingdom). The comparisons of the rates of cancer compared to the rates of benign lesions found *via* the second look biopsy based on risk factors and depth or based on the MRI and ultrasound appearance as per the BIRADS classification were made using the Fisher test. The differences in size on MRI between the benign and malignant nature determined by the second look ultrasound biopsy were measured using the Student's *t*-test.

The comparison of the topography of the lesions between the MRI and the ultrasound was carried out using the Kappa test.

The differences in the measurement of the distance between the lesion and the nipple between the MRI and second look ultrasound and the differences in the measurement of lesion size between the MRI and the second look ultrasound were evaluated using Student's *t*-test.

Results

Of 100 included patients, 108 lesions were detected by MRI, found *via* second look ultrasound and biopsied. 82/108 biopsied lesions (76%) were benign and 26/108 lesions (24%) were malignant. (Fig. 1). Of the benign lesions, 40% (43/108) were fibrous lesions. This high rate could be partially explained by the medical history of the patients (surgery and radiotherapy) (Fig. 2). The proportions of malignant lesions increased with the depth (Fig. 3) without a significant different (Fisher test, $P > 0.78$).

Cancer rates according to the indications

There was not more cancer in the population at risk (patient with a mutation, history of breast cancer at a young age, family history, pre-surgical evaluation), ($n = 20/86$, 23%) than in the population that was not at risk ($n = 7/26$, 27%, Fisher test, $P = 0.7944$). In particular, in patients with a mutation ($n = 5$) or with a family history of breast cancer ($n = 22$), no lesions biopsied on a second look-basis were cancerous. The breast cancer rate was not statistically different in patients with a history of breast cancer at a young age ($n = 7/19$, 37%) compared to the population that was not at risk ($n = 7/31$, 23%, Fisher test, $P = 0.3385$). In case of a local extent evaluation, the rate of additional lesions found on a second look-basis was not statistically higher ($n = 13/41$, 32%) compared to the population that was not at risk ($n = 10/37$, 27%, Fisher test, $P = 0.8043$). Of the clinical indications, two cases of cancer were found in patient for screening for the primary metastatic axillary adenopathy, one case of cancer was found in two patients with discharge from the breast and one case of cancer was found out of five patients with nipple retraction.

Displacement

The study showed that the antero-posterior displacement of lesions is high between the MRI and the ultrasound with moderate agreement between the two methods in terms of the position of lesions in anterior, middle or posterior

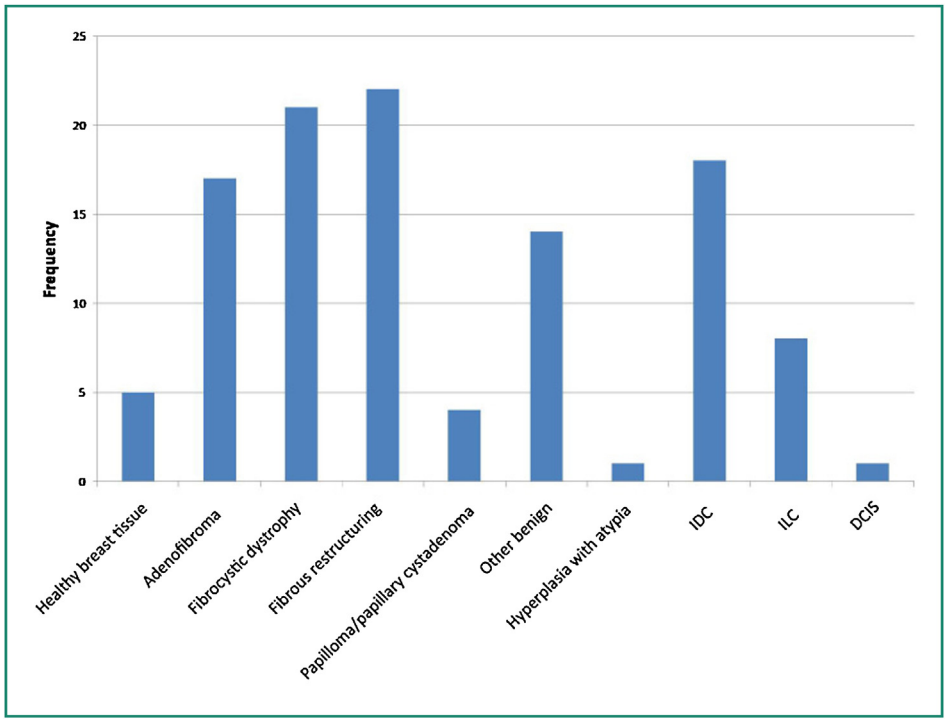


Figure 1. Histogram showing the histological results of the 108 lesions detected on the MRI, found on the second look ultrasound and biopsied. The ''other benign'' classification included: adenosis, cylindrical metaplasia, intraepithelial/intraductal/lobular hyperplasia without atypia, desmoid fibroma.

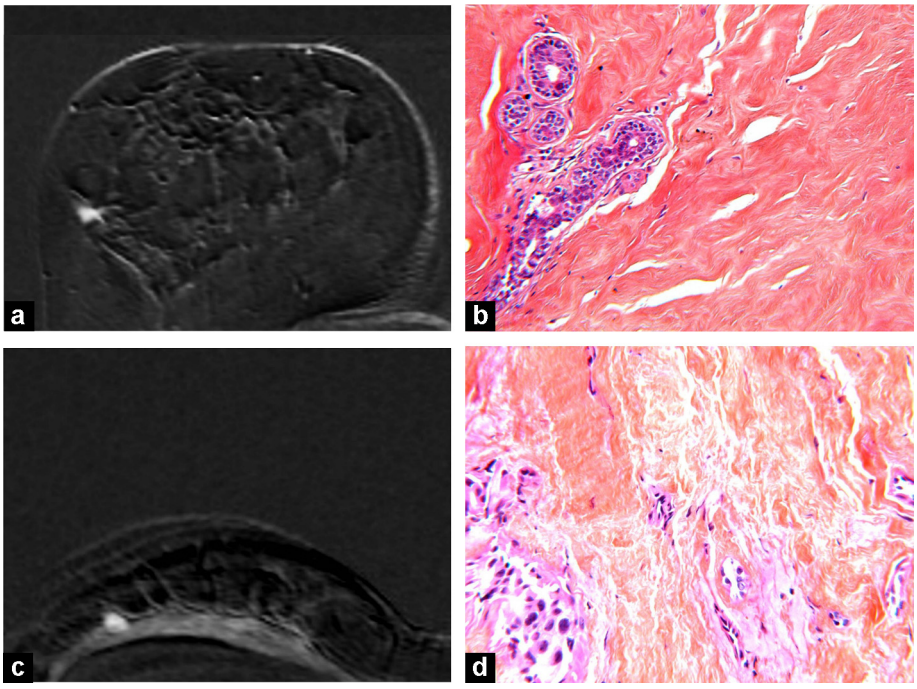


Figure 2. Fibrous lesions upon histological examination. 59-year-old patient with a history of right breast cancer treated with lumpectomy and with homolateral nipple retraction that appeared recently. Discovery of a mass on the MRI with irregular shape and contours, located in the LEQ of the right breast in the mid breast region classified as BIRADS 4 (a, T1 injected with subtraction) corresponding to fibrocystic dystrophy (b). Another 46-year-old patient with a BRCA1 mutation and a history of right breast cancer, with breast implants, followed-up by MRI. Discovery of a mass with regular contours and shape located in the UEQ of the right breast in the deep breast region (c, T1 injected with subtraction) classified as BIRADS 4 due to a type II curve, corresponding to fibrous restructuring with post-radiotherapy nuclear dystrophy (d).

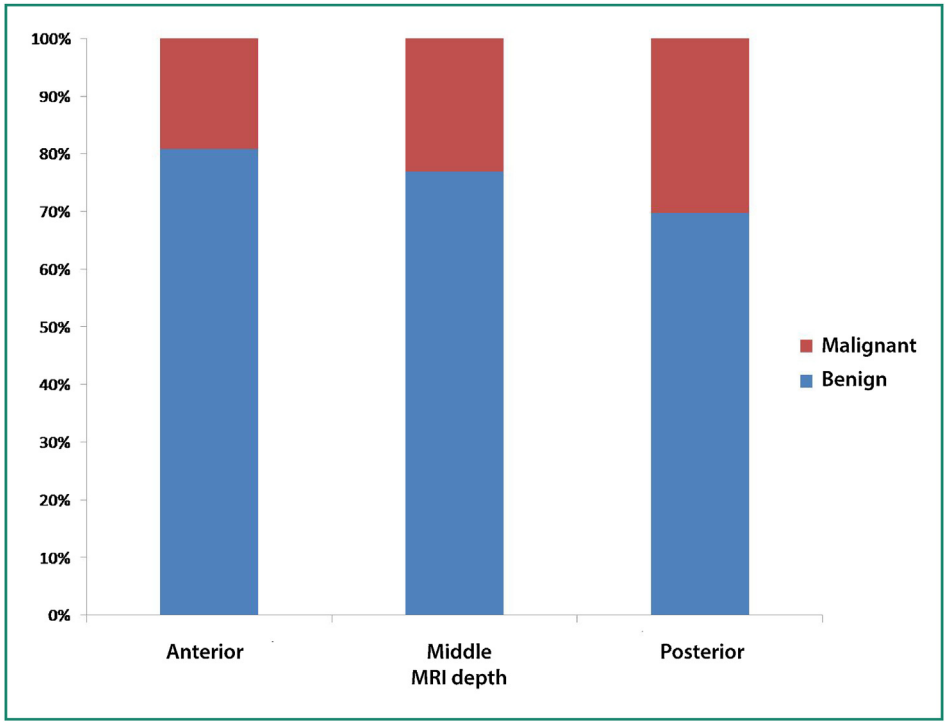


Figure 3. Graphic showing the proportion of malignant and benign lesions based on the breast region where the abnormality is located on the MRI.

breast regions (Kappa = 0.55) (Fig. 4). On the other hand, cranio-caudal displacement of the targets between the MRI and the ultrasound was moderate with almost perfect agreement (Kappa = 0.97) of the topography of the targets in the external and internal quadrants. Moreover latero-median displacement was also moderate with almost perfect agreement agreement (Kappa = 0.93) of the topography of the targets in the external and internal quadrants. The

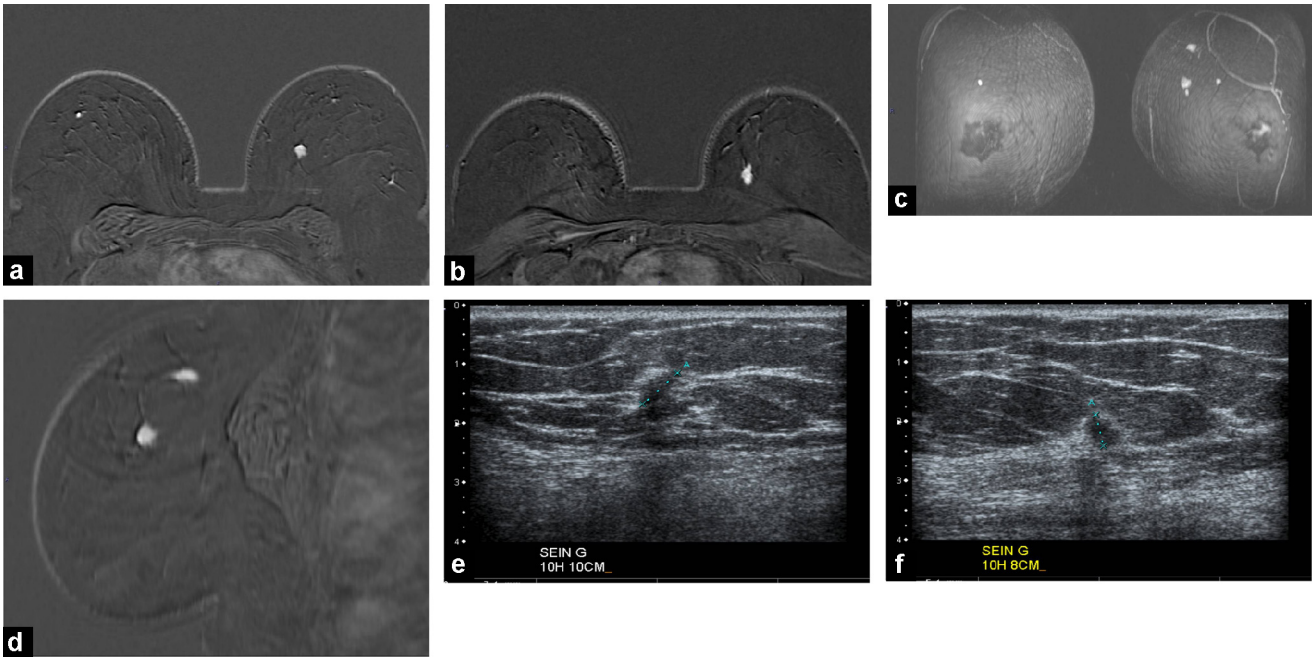


Figure 4. Displacement of lesions between the MRI and the ultrasound. Patient with a history of right breast cancer. Appearance of microcalcifications in the left LEQ with a classification of BIRADS 4 (macrobiopsy planned). MRI carried out for the extension evaluation of the microcalcifications. Discovery on the MRI of two masses in the mid breast region of the UIQ of the left breast in the deep breast zone, with irregular contours and shape classified as BIRADS 4 (a and b, T1 injected with subtraction). The volumetric reconstructions (c) and sagittal MPR (d) of the injected T1 sequence with subtraction show the position of the lesions compared to the level of the skin and the pectoral muscle. In ultrasound, the two masses can be found in the deep breast region in contact with the pectoral muscle (e and f).

comparison of the topography of the targets by quadrant determined by the MRI then by second look ultrasound showed high agreement (Kappa = 0.66). The hour topographic analysis showed a delay of the lesions of more or less 2 hours between the MRI and the ultrasound with moderate agreement between the two methods (Kappa = 0.52). Finally, the MRI overestimated the distance between the target and the nipple compared to the ultrasound (Student *t*-test, $P = 0.04$).

Cancer rate according to the MRI appearance of the lesions

The rate of cancer found by second look ultrasound biopsy was identical for masses and non-masses (19/79 and 7/29, respectively).

For masses, the best criteria for MRI in favour of benignity in this study were benign contours with a negative predictive value (NPV) of 0.86 (regular *versus* spiculated and irregular, Fisher test, $P = 0.0330$, (Fig. 5) and benign enhancement curves VPN = 1 (type I *versus* type II and III, Fisher test, $P = 0.0146$, (Figs. 6 and 7). The T1 appearance, the T2 appearance, the shape and the internal enhancement were not good criteria to predict the type of lesions (Fisher test, $P > 0.0719$). Similarly, the size in MRI did not make it possible to predict the benign character of the lesions (Student's *t*-test, $P = 0.8875$).

For non-masses, the distribution or the internal enhancement did not make it possible to predict the malignant nature of the lesions, Fisher test, $P > 0.5552$ (Fig. 8). The negative predictive values of the BIRADS benign criteria were less than 0.85 for non-masses.

The BIRADS 3 classification on MRI (masses and non-masses) had a negative predictive value of 94% while the positive predictive value of the BIRADS 4 or 5 classification in MRI was 0.27 (Fisher test, $P = 0.0677$ (Fig. 9).

Cancer rate according to the ultrasound appearance of the lesions

The best ultrasound criteria in favour of benignity were the benign shape NPV = 0.90 (round or oval *versus* irregular, Fisher test, $P = 0.0252$), benign contours NPV = 0.91 (circumscribed *versus* irregular or spiculated, Fisher test, $P = 0.0046$) and benign orientation NPV = 0.87 (horizontal *versus* vertical, Fisher test, $p = 0.0018$, (Figs. 8 and 10). The depth of the lesion, echogenicity and the appearance of the posterior ultrasound beam were not good discriminating criteria to predict the malignant or benign character of the lesion (Fisher test, $P > 0.53$). The size on the ultrasound also did not make it possible to predict the benign character of the lesions (Student's *t*-test, $P = 0.6571$).

The BIRADS 3 classification on the ultrasound had a negative predictive value of 95%. The positive predictive value of the BIRADS 4 or 5 classification on the ultrasound was 0.27 (Fisher test, $P = 0.0398$).

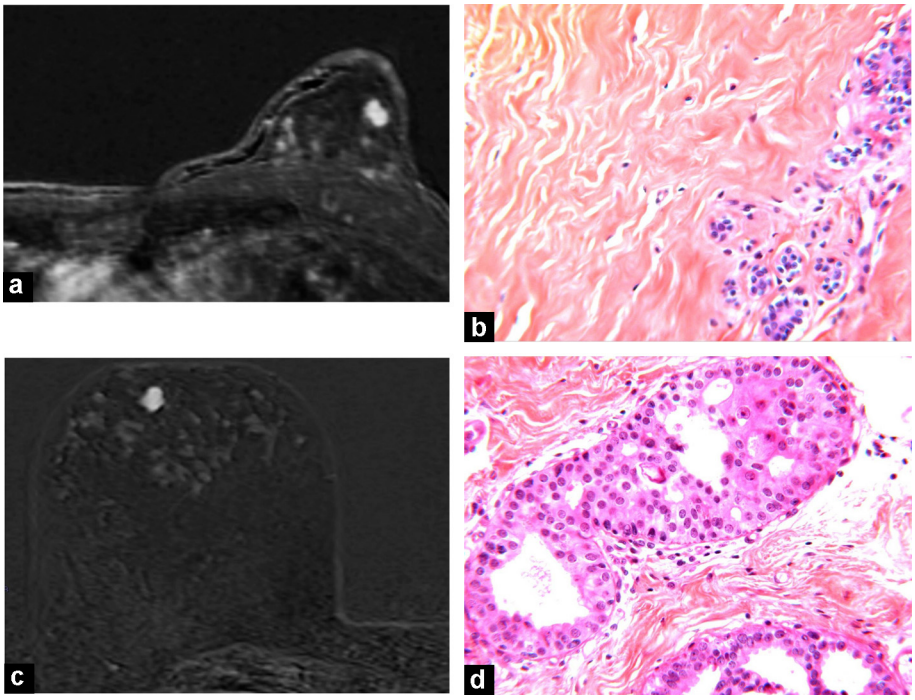


Figure 5. Circumscribed contours *versus* irregular and spiculated contours on MRI. 46-year-old patient with an extension evaluation of right breast cancer for which a mass with irregular shape and circumscribed contours located in the mid breast region of the UEQ of the left breast was discovered on the MRI (a, T1 injected with subtraction). This mass was classified as BIRADS 4. It is a fibrous movement of dystrophic origin (b). Another 53-year-old patient sent for an MRI for the exploration of an architectural distortion of the UEQ of the left breast, for which we discovered a mass of the UEQ of the right breast, located in the anterior breast region, with discreetly irregular shape and two spiculae (c, T1 injected with subtraction). It is a ductal hyperplasia with atypia (d).

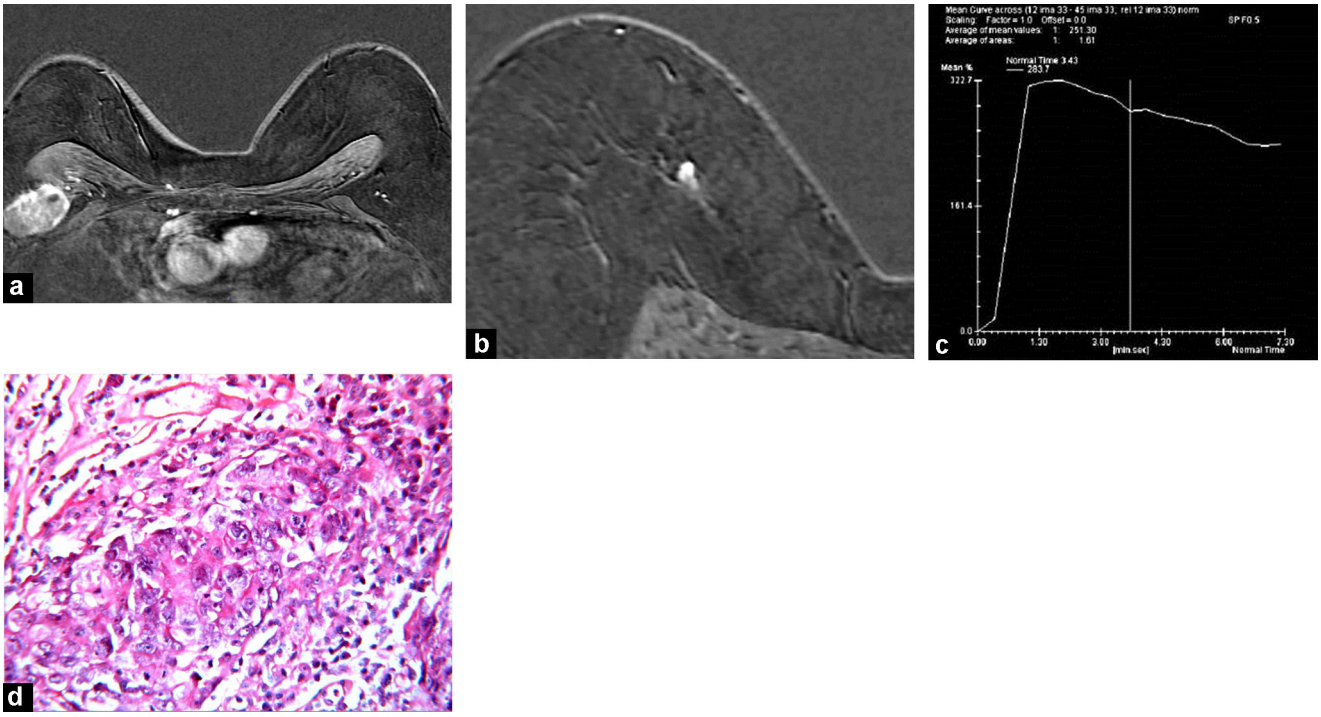


Figure 6. Interest of the curve in MRI when characterising a mass. 69-year-old patient with a right axillar lymph node metastasis of breast cancer (a, T1 injected with subtraction) with a normal first mammography/ultrasound evaluation, screening for the primary tumour on MRI. Discovery of a mass with irregular shape and regular contours (b, T1 injected subtraction), the curve of which shows a wash-out (c), classified as BIRADS 4. It is a grade SBR III invasive ductal adenocarcinoma with a triple negative immunohistochemical profile (d).

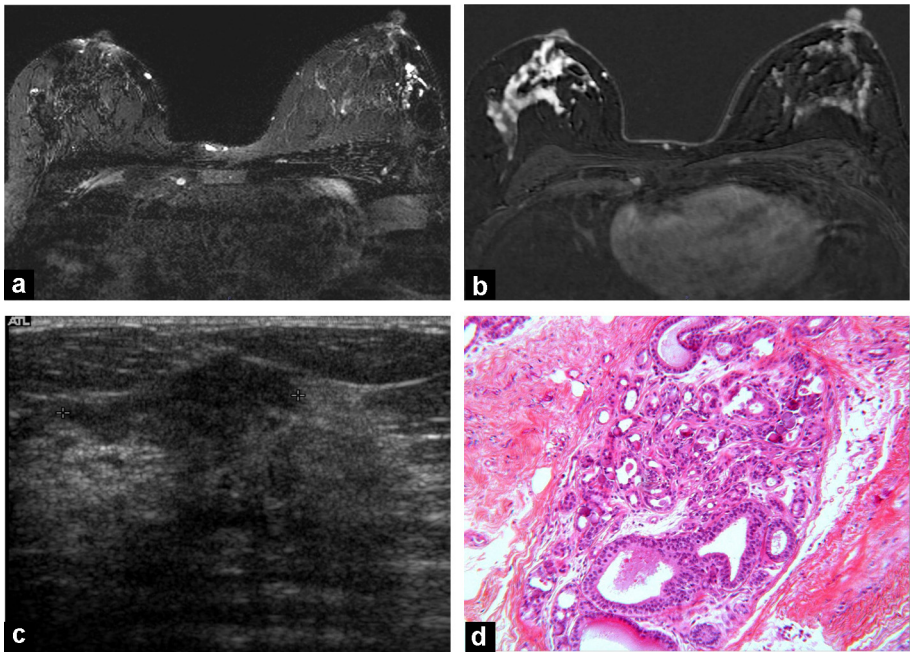


Figure 7. Interest of benign ultrasound contours and the curve in MRI to characterise a mass. 37-year-old patient with a BRCA1 mutation with a personal history of right breast cancer, followed-up by MRI. Appearance of an oval mass with well-circumscribed contours located in the mid breast region of the UIQ of the right breast (a, T1 injected with subtraction) with a type I enhancement curve (b), classified as BIRADS 3. This mass discovered on the MRI corresponds to a mass on the ultrasound that was hypoechogenic, oval, well-circumscribed, with a horizontal orientation, without attenuation, in the mid breast region (c), classified as BIRADS 3. Due to the history of the patient, this mass was biopsied. It was a fibrocystic dystrophy (d).

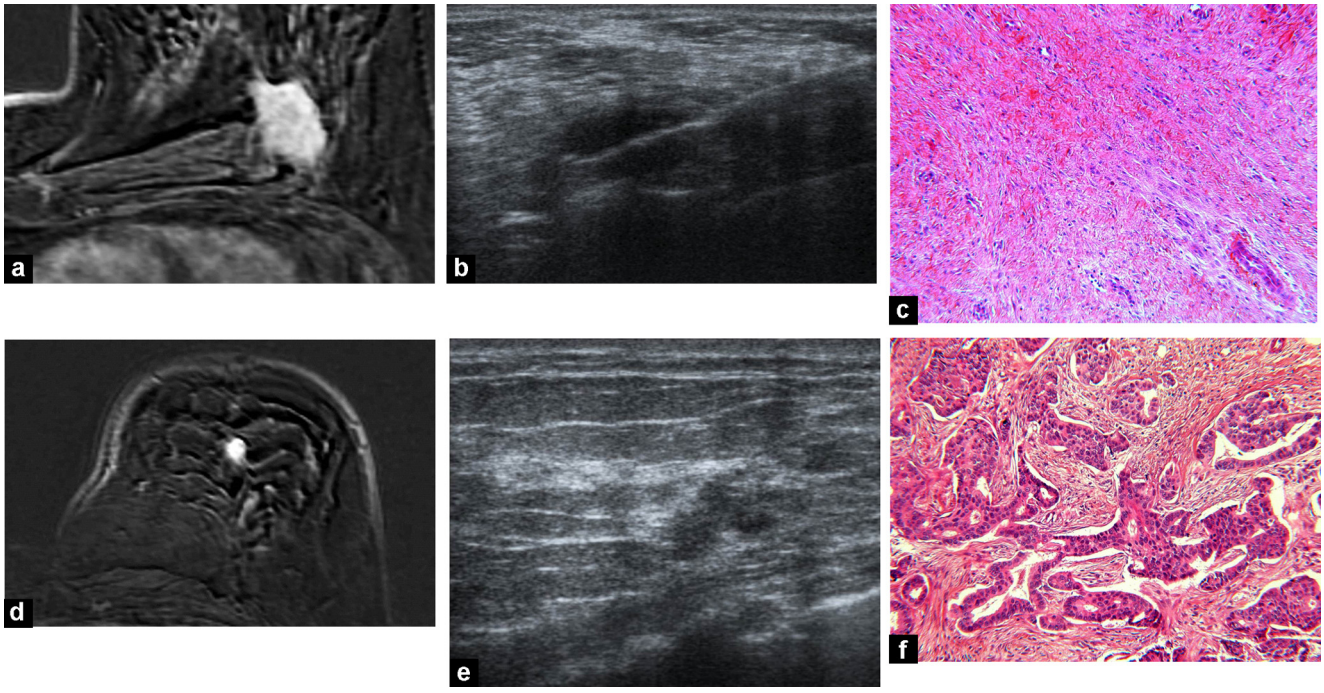


Figure 8. Nonspecific appearance of non-masslike enhancement on MRI. 47-year-old patient with onset of right nipple retraction with mammography and ultrasound without masses or visible calcifications. Discovery on the MRI of enhancement without a segmentary-type homogeneous mass in the JEQ of the right breast classified as BIRADS 4 (a, T2 fat sat, and b, T1 injected with subtraction). On the ultrasound, in the JEQ of the right breast, we found a hypoechogenic mass with irregular contours and shape classified as BIRADS 4 (c). It is a benign sclerosing lesion with adenosis containing microcalcifications (d).

Difference in the appearance of the lesions

Finally, the MRI overestimated the size of the targets compared to ultrasound (Student *t*-test, $P = 0.0001$) (Fig. 11). For masses, the study showed that the agreement in interpretation of the benign *versus* suspicious morphological criteria between the MRI and the ultrasound was very weak for the shape (Kappa = 0.09) and weak for the contours (Kappa = 0.23) (Fig. 12). The BIRADS 3 classification *versus* 4 or 5 was also often different between the ultrasound and the MRI (Kappa = 0.11). The five lesions classified as BIRADS 3 on the MRI and ultrasound were all benign.

Discussion

This study compared the clinical, MRI and second look ultrasound data to the results obtained after biopsy. It showed that the risk factors were not reliable criteria for establishing an indication for second look ultrasound. The lesions found and biopsied on a second look basis were not more often malignant in the population at risk than in the population without any particular risk factors. This study also showed that circumscribed contours and a progressive enhancement curve (type I) for masses on MRI had the strongest negative predictive value of greater than 0.85. For non-masses, the morphological criteria were not discriminating. In ultrasound, the round or oval shape, circumscribed contours and the parallel orientation to the skin favoured benignity with a NPV of greater than 0.85.

The correlation between abnormalities detected on MRI and those found in second look ultrasound or mammography is sometimes delicate [3]. The positioning of the breast is different depending on the imaging method. In MRI, the distance between the chest wall and the glandular tissue is increased by the compression and the procubitus position. The position without compression in decubitus used in ultrasound reduces this distance. In the same way, a slight lateral decubitus is generally used in ultrasound in order to better spread out the breast. Carbonaro *et al.* thus measured by MRI the displacement of lesions between MRI and ultrasound. The switch from procubitus to decubitus could displace the tumour by 30 to 60 mm in the three directions of space. The maximal displacement took place in the antero-posterior direction with displacement of the tumour compared to the level of the sternum of 60 mm and 30 mm compared to the level of the pectoral muscle. On the other hand, according to these authors, the displacement of the lesion compared to the skin or to the nipple was less than 10 mm [4]. The ''hour'' position of the lesion in ultrasound can also vary by one or two hours compared to the MRI. Our results were in complete agreement with these data. It is therefore essential that second look ultrasounds and mammograms be carried out after analysis of MRI images with the help of 3D reconstructions in order to locate the lesion based on relatively ''fixed'' markers, such as the nipple, the skin and unambiguous neighbouring structures (cysts, scars, implant, clips). Our study showed that the interpretation of the shape and the contours of the lesion varied significantly between the MRI and the ultrasound. These results are also in agreement with those in the literature. The shape, size

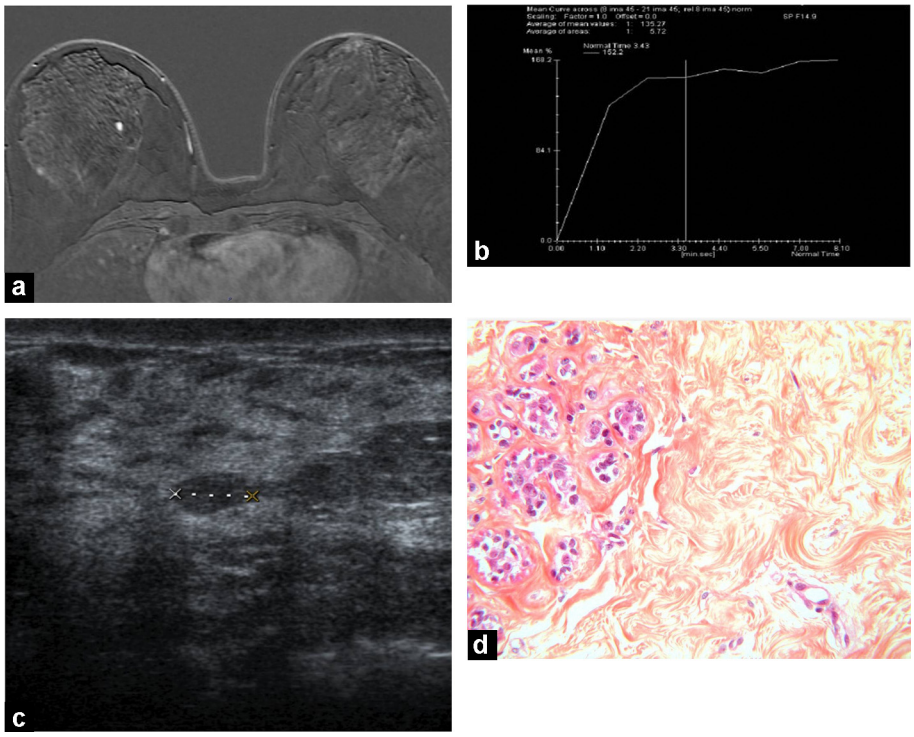


Figure 9. Weak positive predictive value of the BIRADS 4 or 5 in MRI. 60-year-old patient with appearance of left nipple retraction with normal initial mammography and ultrasound. Discovery on the MRI of a mass in the LEQ of the left breast with an irregular shape and spiculated contours in the deep breast region in contact with the pectoral muscle, classified as BIRADS 5 (a) corresponding on the ultrasound to a mass with an irregular shape and spiculated contours also classified as BIRADS 5 (b). It is a benign lesion: a desmoid fibroma (c). Another 57-year-old patient with a personal history of breast cancer with the appearance of a left axillar adenopathy. Discovery of a mass in the JUQ of the left breast with irregular contours and shape located in the mid breast region (d), classified as BIRADS 4, corresponding on the ultrasound to a mass with the same characteristics also classified as BIRADS 4 (e). It is a grade II invasive ductal adenocarcinoma (f).

and contours can be useful in finding a lesion discovered by MRI on second look ultrasound, but perfect agreement must not necessarily be expected [5].

Despite these difficulties related to the switch from MRI to ultrasound, several studies show that it is most often possible to find and biopsy lesions with ultrasound and mammography that were not found using these methods before MRI [5]. The success rate increases for masses (25 to 62%) and decreases for non-masses (11 to 42%) (Fig. 13) [5—7]. The success rate for second look mammographies for non-masses appears to be 19% [2]. Foci with a suspicious character (type III curve) or that are discovered during the local extent evaluation of breast cancer must be looked for in second look ultrasound. These foci are found on second look ultrasound in 46% of cases [8]. Lesions with a highly suspicious appearance on MRI (BIRADS 5) may also be found more often on a second look basis (83%) than classified lesions (BIRADS 4), particularly masses with annular enhancement (75%) and clumped non-masslike enhancement [6,7]. For Meissnitzer [7] and Berg [9], the performance of second look ultrasound could depend on the size of the lesions on the MRI. Ultrasound could thus find 50% of masses measuring less than 5 mm, 56% of masses measuring 6 to 10 mm, 72.5% of masses measuring 10 to 15 mm and 86% of masses measuring more than 15 mm. For non-masses, the performance appears to be 13% for lesions measuring 6 to 10 mm, 25% for those measuring 10 to 15 mm and 42% for those greater than 15 mm (Table 1) [7]. The authors also show that the lesions found on ultrasound appear to be found two or three times more often malignant compared to those found on second look ultrasound and biopsied with a MRI check [7,8]. The ductal carcinoma appear to be found more often on second look ultrasound than *in situ* ductal carcinoma cases or than invasive lobular carcinoma cases [5,7]. Age, the indication of the MRI or the breast density on MRI, does not appear to be criteria that influence the performance of second look ultrasound [8]. These results are in agreement with this study, in which we did not find any link between risk factors for breast cancer and the probability of finding cancer on a second look basis. However, the MRI — ultrasound correlation is not infallible when based only on morphological criteria with an error rate (ultrasound lesions that did not correspond to the MRI) estimated to be 5% of cases in which a cancer could be found in two of three cases [7].

Table 1 Success rate of second look depending on the type of discovered MRI abnormality (mass *versus* non-mass) and its size [7].

Size (mm)	Mass (%)	Non-mass (%)
< 5	50	—
5—10	56	13
10—15	72	25
> 15	86	42

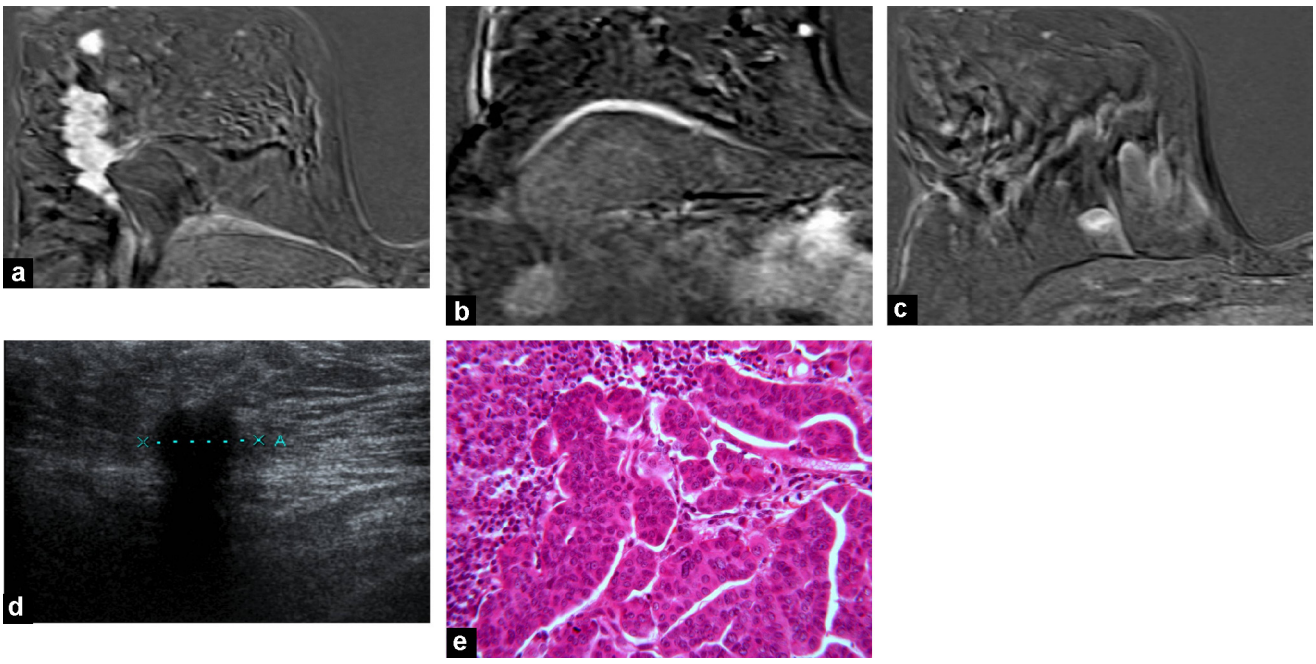


Figure 10. Interest of the orientation of the mass in ultrasound. 44-year-old patient with a luminal invasive ductal carcinoma of the UEQ of the right breast (a) with right axillar adenopathy (b), the biopsy of which indicated a metastasis of a triple negative invasive ductal carcinoma. A breast MRI was thus carried out to screen for a second cancer that went unnoticed. On the MRI, there was an oval mass with regular contours with a type II curve in the JIQ of the right breast located in the deep breast region, classified as BIRADS 4 (c). This abnormality corresponded on the ultrasound to a pre-pectoral, attenuating, oval mass with irregular contours and a non-parallel orientation, classified as BIRADS 4 (d). It was ductal carcinoma with a triple negative invasive immunohistochemical profile (e).

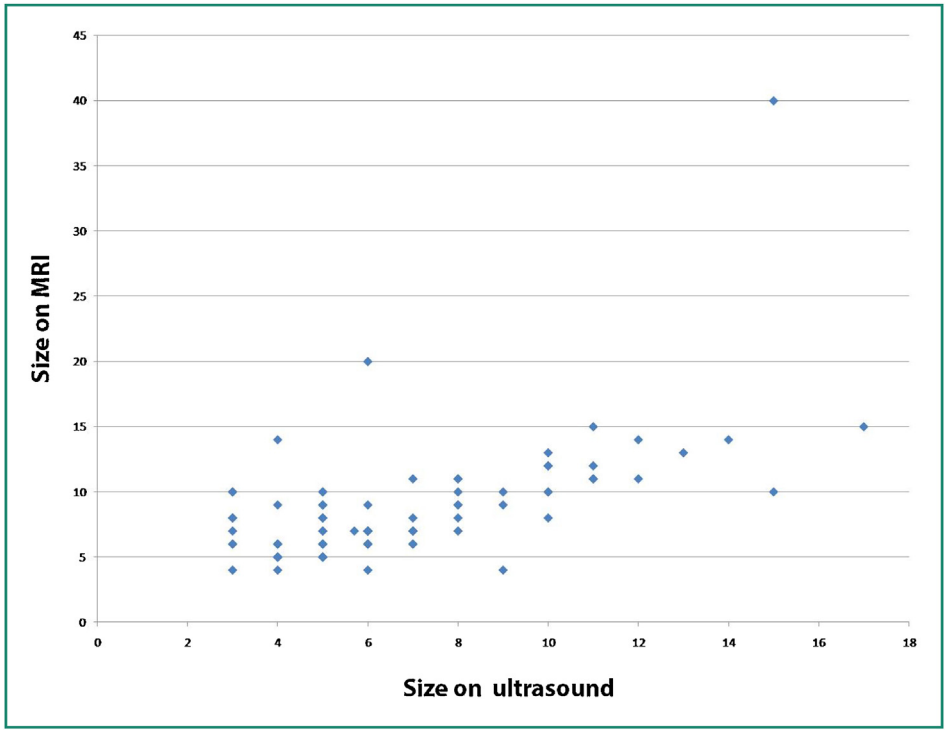


Figure 11. Overestimation of the size of masses by MRI compared to the ultrasound.

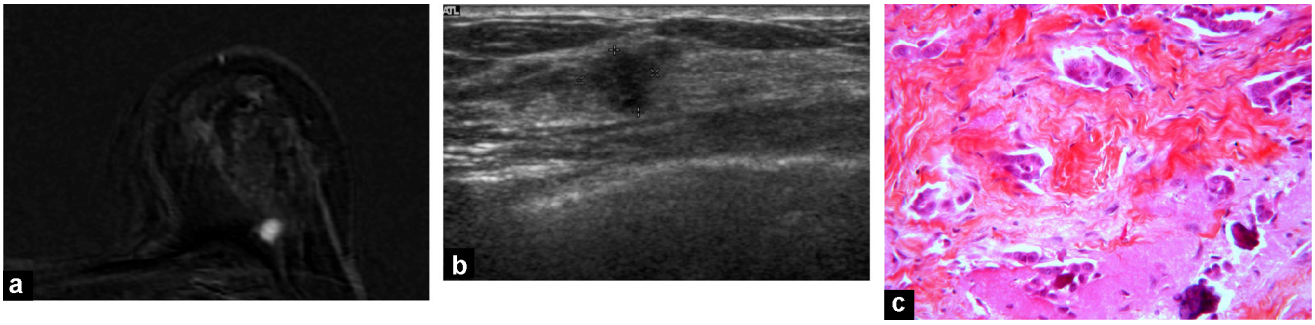


Figure 12. Disagreement concerning morphological criteria between the MRI and the ultrasound. 46-year-old patient with a history of right breast cancer. Discovery on the MRI of a mass in the JLQ of the left breast in the deep breast region with an oval shape and regular contours (a, T1 injected with subtraction) corresponding on the ultrasound to a mass with a vertical orientation and irregular contours and shape classified as BIRADS 4 (b). It is a grade I invasive ductal adenocarcinoma (c).

Cases of cancer discovered in second look ultrasound often have a nonspecific or subtle appearance. According to Abe et al., the lesions could often appear to be benign, round or oval in 60% of cases and isoechogenic in 30% of cases, without a shadow cone in 79% of cases and with a parallel orientation in 60% of cases. According to these same authors, with regard to benign lesions, second look ultrasound may still be capable of distinguishing 63% of them, with the remaining 37% being considered suspicious and a biopsy recommended [8]. On the other hand, for Fiaschetti et al., the negative predictive value of the second look ultrasound in the screening for lesions classified as BIRADS 3 on MRI appears to be 97% [10]. These latest data are in agreement with the results of our study, in which we found a NPV for the ultrasound of 85% for MRI lesions classified as BIRADS 3, 4 and 5. All of the lesions classified as BIRADS 3 on the MRI and ultrasound were benign ($n = 5$). Our study also showed the absence of agreement between the BIRADS classifications obtained by MRI and by ultrasound. This shows that it is absolutely necessary to carry out second look ultrasound

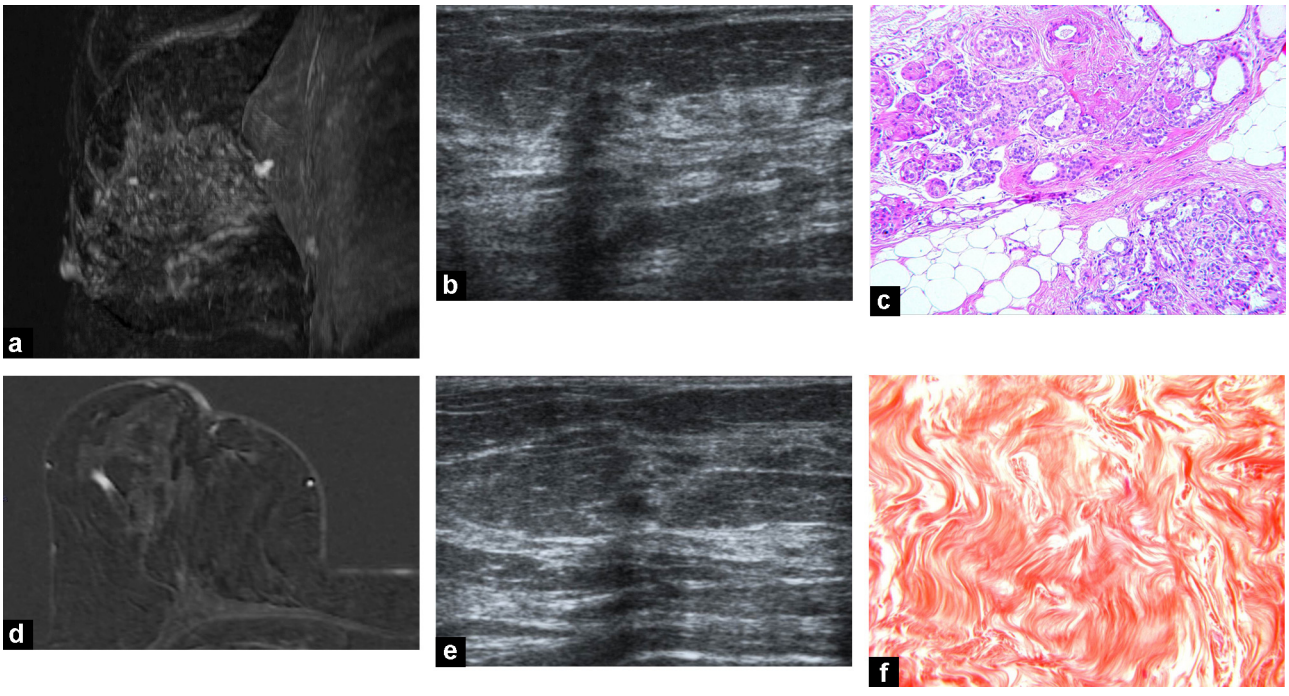


Figure 13. Mass *versus* non-mass success rate of the second look. 60-year-old patient sent for an extension evaluation of an invasive lobular carcinoma in the deep breast region of the right breast. Discovery of a 5 mm mass with an oval shape and circumscribed contours located at the JUQ in the mid breast region of the right breast (a, sagittal cut of an MPR reconstruction of a T1 injected sequence with subtraction). The mass of the JUQ corresponds on the ultrasound to an oval hypoechogenic mass with bi-lobular contours located in the deep breast region (b). It is a fibrocystic dystrophy (c). 60-year-old patient with a family and personal history of right breast cancer, for which a focal area type enhancement without a mass located in the JEQ of the right breast in the mid breast region appeared on the follow-up MRI (d, T1 injected with subtraction). On the ultrasound, this MRI abnormality classified as BIRADS 4 corresponded to a hypoechogenic, oval mass with irregular contours and slightly attenuating, classified as BIRADS 4 (e). It is a scar sclerosis (f).

or mammography for abnormalities classified as BIRADS 3, 4 or 5 on MRI and whose presence changes the treatment of the patient. Indeed, the satellite lesions located near a confirmed tumour do not require any additional investigations as long as the total tumour volume does not exceed 3 cm and/or it does not change the planned surgery. On the other hand, if a lesion is discovered on MRI and it could modify the treatment, this lesion must first be confirmed by a histological control before any decision concerning treatment is made.

In order to improve practices, it is recommended that the correspondence between the lesions biopsied by ultrasound or second look directed stereotaxis after breast MRI be confirmed. For this, it is possible to insert a clip in the biopsy site and to compare its position compared to the target lesion on the MRI using a T1 weighted gradient echo sequence, without fat saturation, that is sensitive to artefacts with magnetic susceptibility (3D rapid EG, TR/TE, 8/4.6; matrix, 276×464; flip angle 16°; voxel size, $0.8 \times 0.8 \times 0.8$ mm) [11]. The echo time can be reduced if the clip to be found is small in order to increase magnetically susceptible artefacts that make it possible to detect the clip. Fat saturation must be avoided, which masks the drop in the signal related to the presence of the clip. The detection of the clip can be disturbed in patients with abundant glandular tissue. If there is disagreement between the biopsy carried out *via* ultrasound and the MRI lesion, a biopsy under MRI should be recommended (Fig. 14).

The limits of this study include the absence of follow-up of non-biopsied patients. This exclusion criteria does not allow us to precisely evaluate the negative predictive values of the morphological criteria in MRI and in ultrasound. A clip was not always inserted during the second look biopsies. However, follow-up for at least two years of patients did not show any targeting errors in the biopsied patients.

There is no consensus concerning the measures to be taken after discovering the MRI lesion *via* second look ultrasound or mammography. Certain teams suggest the following algorithms [2,8] (Figs. 15 and 16).

If confirmation by control MRI of the position of the clip implanted during the biopsy is obtained, in case of a benign

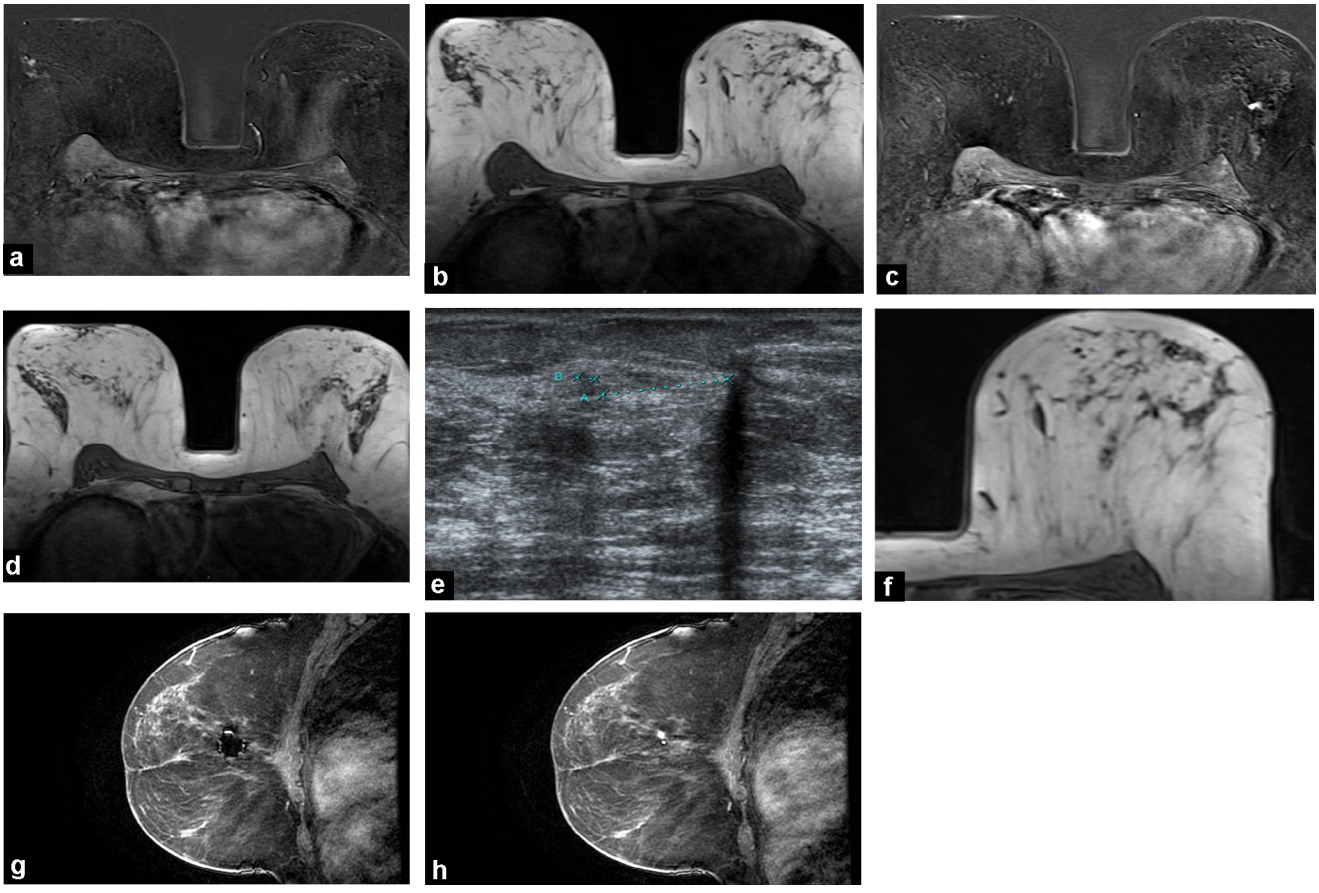
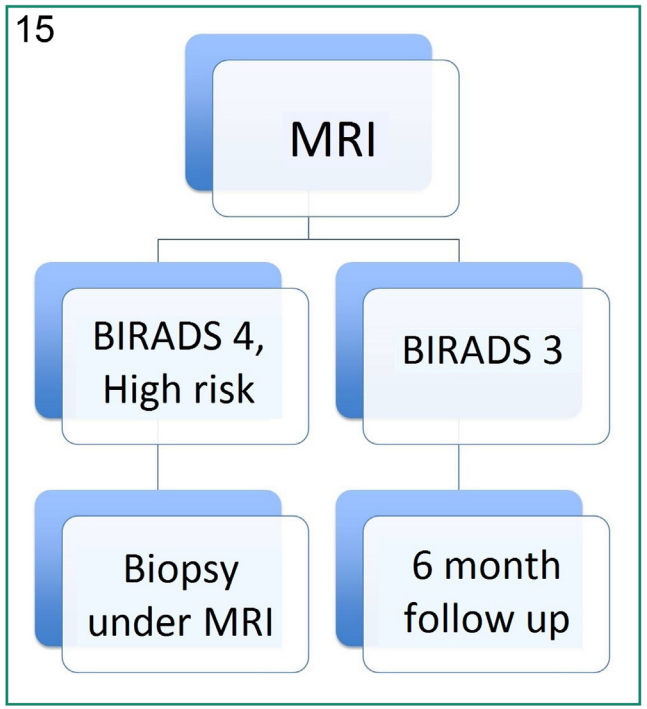
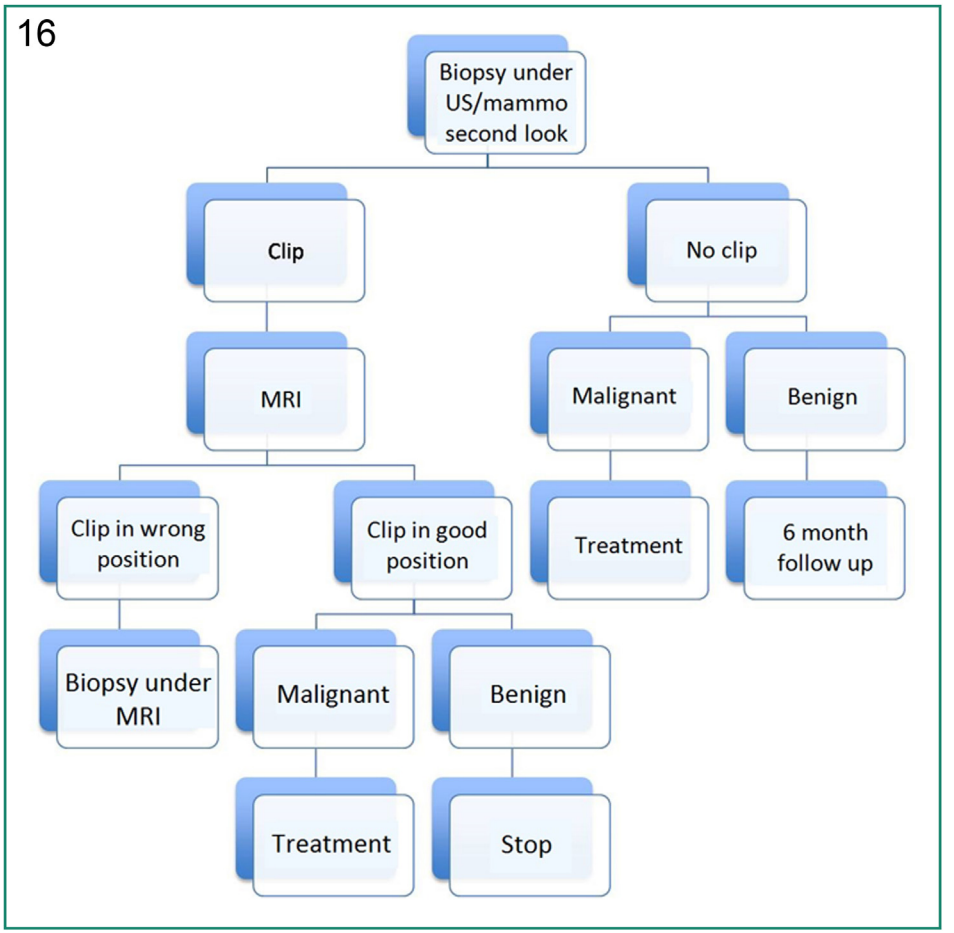


Figure 14. Clip. Extension evaluation of an CLI of the UEQ of the right breast (a, injected T1 with subtraction, and b, T1 non-injected) in a patient with a BRCA 1 mutation with a history of triple negative CCI of the left breast. The MRI makes it possible to discover a retro-areolar mass in the deep breast region of the left breast, with irregular contours and shape (c, T1 injected with subtraction, c, T1 non-injected). This mass, which is classified as BIRADS 4, corresponds on the ultrasound to a hypoechogenic mass with irregular shape and spiculated contours, located in the mid breast region, classified as BIRADS 5 (e). A biopsy was carried out with the implantation of a clip at the end of the procedure. The position of the clip was then controlled by MRI. The visualized clip is much more anterior than the suspicious lesion was on the MRI (f). A new biopsy was thus carried out under MRI (g and h). It is an invasive lobular carcinoma associated with an *in situ* lobular carcinoma.





Figures 15 and 16. Algorithms concerning the measures to be taken after discovery on second look mammography or ultrasound of an MRI lesion.

histological result, MRI follow-up is not absolutely necessary. If the biopsy is carried out outside the MRI target, a biopsy under MRI is then recommended. If the confirmation by control MRI of the clip is not possible, in case of a benign second look ultrasound histological result, follow-up must be carried out six months after the biopsy in MRI [2].

In case of a lesion with a typically benign appearance on second look ultrasound or mammography (lymph node with a fatty hilum, cytosteatonecrosis), if no sample is taken, the lesion must be classified as BIRADS 3 and controlled 6 months later. Indeed, the risk of cancer appears to be reduced in this situation (less than 1%). The choice of the follow-up method remains debatable. The conferences of current consensus do not recommend MRI in this indication and ''standard'' follow-up by mammography with or without ultrasound is justified [12—14].

If the lesion is not found on ultrasound or mammography and if it has a benign appearance on MRI, it can be classified BIRADS 3 and monitored by MRI. In the absence of a suspicious MRI lesion on the second look ultrasound, in particular in a patient at high risk, the performance of an MR-guided biopsy is recommended [5,6,15].

TAKE-HOME MESSAGES

- Good MRI—ultrasound agreement in terms of localisation.
- Masses found better than non-masses.
- BIRADS 5 found better than BIRADS 4.
- The biopsy indications must be wide with insertion of a clip and a control MRI.
- Risk factors are not reliable criteria for the indication of second look ultrasound.
- For masses in MRI, circumscribed contours and progressive type I enhancement have the strongest negative predictive value (greater than 85%).
- For masses in ultrasound, a round or oval form, circumscribed contours and an orientation parallel to the skin have the strongest negative predictive value.

Clinical case

A 45-year-old patient is sent for an MRI for a local extent evaluation of left breast cancer. Fig. 17a shows the injected

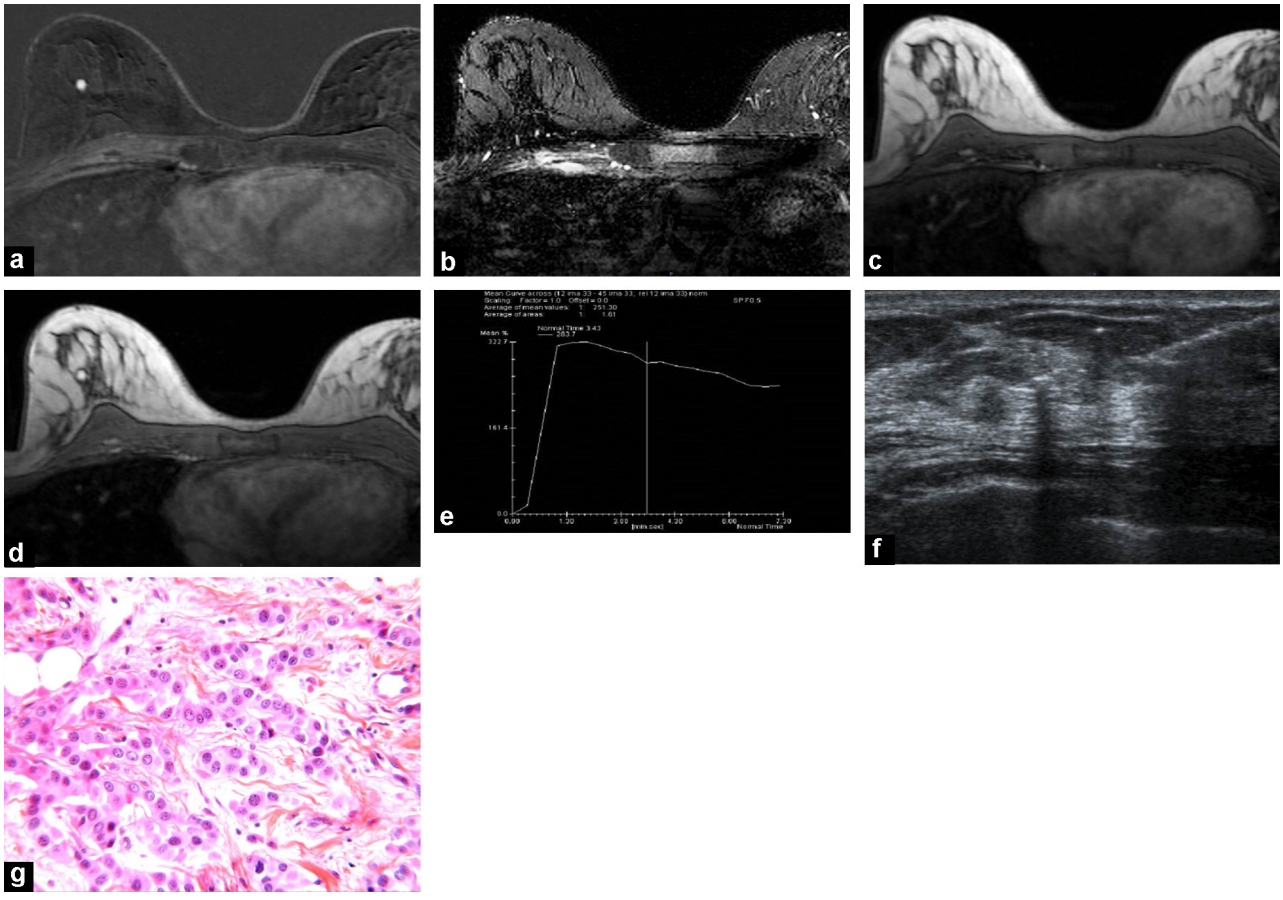


Figure 17. 45-year-old patient sent for an MRI for a local extent evaluation of left breast cancer. There's a mass with a T2 hypersignal and T1 isosignal. It is located at the UEQ of the left breast in the mid breast region. Injected T1 with subtraction (a), T2 with fat signal saturation (b), T1 without injection (c) and T1 with injection (d). Based on the morphological criteria alone, the mass should be classified as BIRADS 3, but the enhancement curve is a type III (e), so the mass is classified as BIRADS 4. On the ultrasound it corresponds to a mass with irregular contours and shape, without posterior attenuation (f). The mass was biopsied and turned out to be a synchronous contralateral cancer of the grade II invasive ductal carcinoma type (g).

T1 with subtraction, Fig. 17b shows the T2 with fat signal saturation, Fig. 17c shows the T1 without injection and Fig. 17d shows the T1 with injection.

Questions

1. Based on the provided images, what abnormality should be described? What is its BIRADS classification based on these morphological criteria?
2. Fig. 17e is an additional aspect of the MRI. What is it? What does it mean?
3. Fig. 17f shows the ultrasound image of the abnormality discovered on the MRI. The abnormality discovered on the MRI corresponds on the ultrasound to a mass with irregular contours and shape, without posterior attenuation, located in the deep breast region. What is its BIRADS in ultrasound?

Answers

1. Response: it is a mass with a T2 hypersignal and T1 isosignal. It is located at the UEQ of the left breast in the mid breast region. It has a round shape with circumscribed contours. It is classified as BIRADS 3 based on the morphological criteria alone.
2. Response: it is the enhancement curve of the mass. It has a wash-in and a wash-out. It is a type III curve. This negative functional criteria is added to the previously mentioned benign morphological criteria. The mass therefore becomes suspicious and is thus classified as BIRADS 4.
3. Response: the mass is classified as BIRADS 4.

The mass was biopsied and turned out to be a synchronous contralateral cancer of the grade II invasive ductal carcinoma type (Fig. 17g). The treatment of the patient will therefore be modified.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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